Translation

PATENT COOPERATION TREATY

PCT/JP2003/014559

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference R-36	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/014559	International filing date (*day/month/year*) 17 November 2003 (17.11.2003)	Priority date (*day/month/year*) 18 November 2002 (18.11.2002)
International Patent Classification (IPC) or national classification and IPC A61K 45/06, 31/138, 31/343, 31/353, 31/437, 31/4409, 31/4412, 31/496, 31/5377, 31/551, A61P 27/06, 43/00		
Applicant SANTEN PHARMACEUTICAL CO., LTD.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☒ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 June 2004 (14.06.2004)	06 October 2004 (06.10.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/014559

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ The international application as originally filed/furnished

☐ the description:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

pages _____, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the drawings:

pages _____, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

ernational application No.
PCT/JP2003/014559

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 5-8

because:

☒ the said international application, or the said claims Nos. 5-8 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

SEE SUPPLEMENTAL SHEET

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 5-8 .

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: III.1

The inventions that are set forth in claims 5 to 8 pertain to methods for the treatment of the human body by therapy (PCT Article 34(4)(a)(i) and PCT Rule 67.1(iv)).

INTERNATIONAL [redacted]ELIMINARY EXAMINATION REPORT

[redacted]rnational application No.
PCT/JP 03/14559

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-4, 9-12	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-4, 9-12	NO
Industrial applicability (IA)	Claims	1-4, 9-12	YES
	Claims		NO

2. Citations and explanations

The present written opinion was drafted on the basis of the disclosures of the following documents, which are cited in the international search report.

Document 1: EP 1034793 A1 (Senju Pharmaceuticals Co., Ltd.)

Document 2: EP 956865 A1 (Yoshitomi Pharmaceutical Ind., Ltd.)

Document 3: UEHARA, M. et al., Nature, 1997, 389, pp. 990 to 994

Document 4: WO 97/23222 A1 (Alcon Laboratories, Inc.)

Document 5: Mariko ASAHI et al., The Pharmaceuticals Monthly, 1996, 38 (9), pp. 2311 to 2331

Document 6: Kuniteru SHIRATO, Ganka, 2002, 44 (11), pp. 1443 to 1448

Document 7: Tatsuro FUKUCHI, Ganka, 2002, 44 (11), pp. 1458 to 1463

Document 8: WO 02/38158 A1 (PHARMACIA AB)

Document 9: WO 93/16701 A2 (Alcon Laboratories, Inc.)

Document 10: EP 286903 A1 (The Trustees of Columbia)

Document 11: Ikuro HIGASHI et al., The Journal of the Eye, 2002, 19 (2), pp. 261 to 266

Document 12: Yuichiro OTAKE et al., The Journal of the Eye, 2000, 17 (5), pp. 687 to 690

Claims 1 to 4 and 9 to 12

Document 1 discloses agents for the treatment of glaucoma, which comprise a Rho kinase inhibitor as the active component, while documents 1 to 4 disclose specific compounds that exhibit a Rho kinase-inhibiting activity. Therein, a comparison of the inventions that are set forth in claims 1 to 4 and 9 to 12 and the inventions that are disclosed in documents 1 to 4 shows that the inventions set forth in claims 1 to 4 and 9 to 12 comprise a mixture of a Rho kinase inhibitor and a β-blocker; therefore, the former inventions differ from the latter inventions.

However, the fact that it is possible to use β-blockers in the treatment of glaucoma would be well known to a person skilled in the art, as disclosed in documents 5 to 12, and the feature of combining β-blockers with other medicaments that exhibit a therapeutic action in relation to glaucoma in order to achieve a more favorable therapeutic action would also be well known to a person skilled in the art. Therefore, it cannot be said to require special creative ability for a person skilled in the art to attempt to combine β-blockers and the Rho kinase inhibitors that are disclosed in documents 1 to 4 with the expectation of achieving a more favorable therapeutic action.

Consequently, the inventions that are set forth in claims 1 to 5 and 9 to 12 do not involve an inventive step in the light of documents 1 to 12.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
WO 03/049745 A1 [E, X]	19 June 2003 (19.06.2003)	12 December 2002 (12.12.2002)	12 December 2001 (12.12.2001)

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1 to 4 and 9 to 12

Claims 1, 2, 9 and 10 disclose Rho kinase inhibitors and β-blockers as the components of agents for the treatment of glaucoma. However, it is unclear specifically what compounds are included within the scope of the Rho kinase inhibitors, and β-blockers include a wide and varied range of compounds; consequently, it would be difficult to conduct an exhaustive examination in relation to all of the components in question. In addition, the disclosures of the description only set forth one specifically used compound for each of the components in the agents, and do not confirm the effects that result from combinations of other component compounds. Therefore, the inventions that are set forth in the present application cannot be said to be fully disclosed or to be fully supported by the description in the meaning of PCT Articles 5 and 6.

Consequently, the present written opinion was drafted only in relation to the scope of the items which are disclosed in each of the documents that are cited in the international search report.